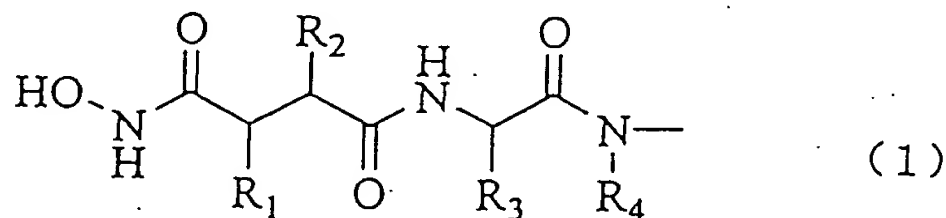


CLAIMS

1. A conjugate of (1) at least one therapeutic agent for joint diseases and (2) hyaluroic acid, a hyaluroic acid derivative or a salt thereof.
2. The conjugate of claim 1, wherein the bond between at least one therapeutic agent for joint diseases and hyaluroic acid, a hyaluroic acid derivative or a salt thereof is a covalent bond.
3. The conjugate of claim 1 ~~or 2~~, wherein the therapeutic agent for joint diseases is a matrix metalloprotease inhibitor.
4. The conjugate of ~~any one of claims 1 to 3~~, wherein the matrix metalloprotease inhibitor binds to hyaluroic acid, a hyaluroic acid derivative or the salt thereof via a spacer.
5. The conjugate of ~~any one of claims 1 to 4~~, wherein the weight ratio of the matrix metalloprotease inhibitor to the entire conjugate is 0.01 to 50%.
6. The conjugate of ~~any one of claims 1 to 5~~, wherein the matrix metalloprotease inhibitor is a hydroxamic acid residue.
7. The conjugate of ~~any one of claims 1 to 6~~, wherein the matrix metalloprotease inhibitor is a hydroxamic acid residue represented by the general formula (1):



wherein

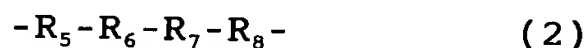
R₁ is a hydrogen atom, a hydroxyl group or a straight-chain or branched-chain alkyl group having 1 to 8 carbon atoms;

R₂ is a straight-chain or branched-chain alkyl group having 1 to 8 carbon atoms;

R₃ is a straight chain or branched alkyl group having 1 to 8 carbon atoms which may be substituted with a cycloalkyl group, an aryl group or a heterocyclic group; and

R₄ is a hydrogen atom or an alkyl group having 1 to 4 carbon atoms.

8. The conjugate of ~~any one of claims 1 to 7~~, wherein the spacer is represented by the general formula (2):



wherein

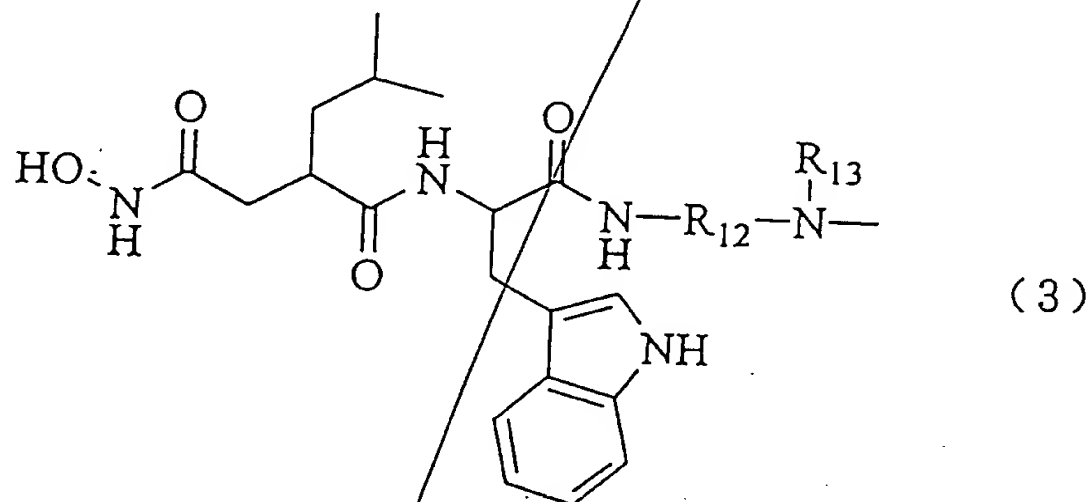
R₅ is a straight-chain or branched-chain alkylene group having 1 to 8 carbon atoms;

R₆ is an oxygen atom or a methylene or imino group which may be substituted with a straight-chain or branched-chain alkyl group having 1 to 4 carbon atoms;

R₇ is a straight-chain or branched-chain alkylene group having 1 to 10 carbon atoms into which one to three oxygen atoms may be inserted; and

R₈ is an oxygen atom, a sulfur atom or NR₉, wherein R₉ is a hydrogen atom or a straight-chain or branched-chain alkyl group having 1 to 4 carbon atoms.

9. The conjugate of ~~any one of claims 1 to 8~~, wherein the conjugate of the matrix metalloprotease inhibitor and the spacer is represented by the general formula (3):



wherein

R_{12} is a straight-chain or branched-chain alkylene group having 2 to 23 carbon atoms into which one imino group and/or one to four oxygen atoms may be inserted; and

R_{13} is a hydrogen atom or a straight-chain or branched-chain alkyl group having 1 to 4 carbon atoms.

10. The conjugate of ~~any one of claims 1 to 9~~, wherein the matrix metalloprotease inhibitor in the form of a conjugate with hyaluroic acid, a hyaluroic acid derivative or a salt thereof inhibits a matrix metalloprotease *in situ*.

11. A method for preparing the conjugate of ~~any one of claims 1 to 10~~ comprising binding a site of the therapeutic agent for joint diseases that does not affect the activity of the agent to a carboxyl group, a hydroxyl group or a

functional group at the reducing end of hyaluroic acid, a hyaluroic acid derivative or a salt thereof by direct chemical reaction or via a spacer.

12. A pharmaceutical composition comprising the conjugate of ~~any one of claims~~ 1 to 10.

13. The pharmaceutical composition of claim 12 which is a therapeutic agent for joint disease.

14. The pharmaceutical composition of claim 13, wherein the joint disease is osteoarthritis, rheumatoid arthritis or scapulohumeral periarthrititis.

15. The use of the conjugate of ~~any one of claims~~ 1 to 10 in the preparation of a pharmaceutical composition.

16. The use of ~~the~~ conjugate of ~~any one of claims~~ 1 to 10 in the preparation of a therapeutic agent for joint diseases.

17. A method for treating a patient having a joint disease comprising administering a pharmaceutical composition containing a pharmaceutically effective amount of the conjugate of ~~any one of claims~~ 1 to 10 as the effective ingredient to the patient.

add B4 >